CLAIMS

1. (original) Library comprising a plurality of tagged ligands of formula I

$$(Lig\ J_L)_m\ L\ (J_T\ Tag)_m\ (J_T\ L\ (J_L\ Lig)_m)_p$$

and salts thereof wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers
comprising one or a plurality of same or different ligand moieties Lig each linked to one or a plurality of same or different tag moieties Tag via same or different linker moieties L and same or different linking site or linking functionality J_T and J_L
wherein Lig comprises a GPCR ligand, an inhibitor of an intracellular enzyme or a substrate or inhibitor of a drug transporter;

L is selected from a double bond, -O-, -S-, amine, COO-, amide, -NN- hydrazine; and saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}600}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, wherein optional substituents are selected from any $C_{1\text{-}20}$ aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano and carbonyl and combinations thereof, and L may be monomeric, oligomeric having oligomeric repeat of 2 to 30 or polymeric having polymeric repeat in excess of 30 up to 300;

Tag is any tagging substrate;

m are each independently selected from a whole number integer from 1 to 3;

p is 0 to 3

wherein one or more of each -Tag in one or more or each library compound is a fluorophore entity -Fl, whereby the library comprises compounds of which one or more or all of which are of formula I'
$(LigJ_L)_m\ L\ (J_T\ Fl)_m\ (J_T\ L\ (J_L Lig)_m)_p$
characterised in that linking is at same or different linking sites in compounds comprising different Lig, J_L, L J_T and/or – Tag and is at different linking sites in compounds comprising same Lig, J_L, L J_T and/or – Tag
with the proviso that when Lig is CGP12177 and L is 1,1,4,4-tetramethyl butylamine $C(CH_3)_2(CH_2)_2C(CH_3)_2NH$-, Fl is not BODIPY® FL, or when L is $C(CH_3)_2(CH_2)_2$-$C(CH_3)_2NHCSNH$ – then Fl is not FITC, eosin or erythrosin.

2. (original) Library comprising a plurality of tagged ligands of formula I

$$(Lig\ J_L)_m\ L\ (J_T\ Tag)_m\ (J_T\ L\ (J_L\ Lig)_m)_p$$

and salts thereof wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers
comprising one or a plurality of same or different ligand moieties Lig each linked to one or a plurality of same or different tag moieties Tag via same or different linker moieties L and same or different linking site or linking functionality J_T and J_L

wherein Lig comprises a GPCR ligand, an inhibitor of an intracellular enzyme or a substrate or inhibitor of a drug transporter;

L is selected from a double bond, -O-, -S-, amine, COO-, amide, -NN- hydrazine; and saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}600}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, wherein optional substituents are selected from any $C_{1\text{-}20}$ aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano and carbonyl and combinations thereof, and L may be monomeric, oligomeric having oligomeric repeat of 2 to 30 or polymeric having polymeric repeat in excess of 30 up to 300;

Tag is any tagging substrate;

m are each independently selected from a whole number integer from 1 to 3;

p is 0 to 3

wherein one or more of each -Tag in one or more or each library compound is a fluorophore entity -Fl, whereby the library comprises compounds of which one or more or all of which are of formula I'

$(LigJ_L)_m$ L $(J_T\ Fl)_m$ $(J_T$ L $(J_L Lig)_m)_p$

wherein linking is at same or different linking sites in compounds comprising different Lig, J_L, L J_T and/or – Tag and is at different linking sites in compounds comprising same Lig, J_L, L J_T and/or – Tag

with the proviso that when Lig is CGP12177 and L is 1,1,4,4-tetramethyl butylamine $C(CH_3)_2(CH_2)_2C(CH_3)_2NH$-, Fl is not BODIPY® FL, or when L is $C(CH_3)_2(CH_2)_2$-$C(CH_3)_2NHCSNH$ – then Fl is not FITC, eosin or erythrosin

characterised in that the or each Fl is selected from a red, near ir or blue absorbing dye or from BODIPY® 630/650 or BODIPY® 630/650 X.

3 (currently amended) Library as claimed in ~~any of~~ Claims 1 ~~to 2~~ wherein each compound of formula I or I' comprises one of a plurality of fluorophores and/or tags providing a library of differently fluorescently tagged ligands comprising one or a number of different fluorophores optionally of different chemical composition or spectral characteristics; and/or providing a library of differently tagged ligands including at least one fluorescently tagged ligand; alternatively each compound of formula I or I' comprises one of a plurality of precursor ligands linked each to one or a plurality of different tags providing a library of same or differently tagged ligands of plural ligand type; alternatively each compound of formula I comprises one of a plurality of linkers linking a precursor ligand and at least one Tag at the same or different linking site; alternatively each compound of formula I comprises the same linker linking a precursor ligand and at least one Tag at different linking sites providing a library of differently linked tagged ligands of different conformation or anticipated pharmacology and binding.

4 (currently amended) Library as claimed in ~~any of~~ Claims 1 ~~to 3~~ comprising a plurality of compounds of one or more of formula II to III:

II $(LigJ_L)_m$ L J_T TagJ_T L $(J_L$ Lig$)_m$ where each m is as hereinbefore defined and is preferably 1 or 2, more preferably 1

III $(LigJ_L)_m$ L $(J_TTag)_m$ wherein each m is as hereinbefore defined and is preferably 1 and/or 2, more preferably

Lig J_L – L – J_L Tag and/or

Lig J_L – L – J_T Tag and/or Lig J_L – L – J_T Tag

$\diagdown J_L$ Lig $\diagdown J_T$ Tag

wherein each J_L and J_T comprises J as hereinbefore defined and may be same or different and may derive from functionality originally present in Lig or L and Tag or L or a combination thereof, characterised in that linking is at same or different linking sites in compounds comprising different Lig, J_L, L, J_T and/or Tag, and is at different linking sites in the case of any two or more compounds comprising identical Lig, J_L, L, J_T and/or Tag.

5 (currently amended) Library as claimed in ~~any of~~ Claims 1 ~~to 4~~ including information for each compound of formula I comprised in the Library, relating to the pharmacology for binding to or inhibition of a GPCR receptor or to inhibition of an intracellular cyclic nucleotide phosphodiesterase, or inhibition of or transport by a drug transporter including designation as agonist, antagonist, substrate or inhibitor and measure of affinity or inhibition, enabling quantification of results.

6 (currently amended) Library as claimed in ~~any of~~ Claims 1 ~~to 5~~ wherein a GPCR ligand is selected from any compound which is effective as an agonist or antagonist for an adenosine receptor, a beta-adrenoceptor, a muscarinic receptor, a histamine receptor, an opiate receptor, a cannabinoid receptor, a chemokine receptor, an alpha-adrenoceptor, a GABA receptor, a prostanoid receptor, a 5-HT (serotonin) receptor, an excitatory aminoacid receptor (glutamate), a dopamine receptor, a protease-activating receptor, a neurokinin receptor, an angiotensin receptor, an oxytocin receptor, a leukotriene receptor, a nucleotide receptor (purines and pyrimidines), a calcium-sensing receptor, a thyroid-stimulating hormone receptor, a neurotensin receptor, a vasopressin receptor, an olfactory receptor, a nucleobase receptor (adenosine), a lysophosphatidic acid receptor, a sphingolipid receptor, a tyramine receptor (trace amines), a free-fatty acid receptor and a cyclic nucleotide receptor; an inhibitor of intracellular enzymes is an inhibitor of cyclic nucleotide phosphodiesterases; and a substrate or inhibitor of a drug transporter is selected from a substrate or inhibitor of an equilibrium based drug transporter or ATP driven pump selected from a catecholamine transporter, a nucleoside transporter, an ATP-binding cassette transporter, a cyclic nucleotide transporter or derivatives or analogues thereof ;

or wherein Lig is selected from

a) xanthine like structures including XAC, theophylline, caffeine, theobromine, dyphilline, enprofylline; or fused biaryl structures including papaverine, dihydroquinilones, cilostamide, dipyridamole or vinpocetine; and analogues thereof;

b) adenosine like structures including ADAC, NECA and analogues thereof;

c) ethanolamine like structures including salmeterol, salbutamol, terbutaline, quinprenaline, labetalol, sotalol, bambuterol, fenoterol, reprotolol, tulobuterol, clenbuterol and analogues thereof;

d) oxypropanolamine like structures including CGP12177, propranolol, practolol, acebutalol, betaxolol, ICI 118551, alprenolol, celiprolol (celectol), metoprolol (betaloc), CGP20712A, atenolol, bisoprolol, misaprolol, carvedilol, bucindolol,

esmolol, nadolol, nebivolol, oxprenolol, xamoterol, pindolol, timolol and analogues thereof;

e) xanthine like structures including XAC, theophylline, caffeine, theobromine, dyphilline, enprofylline, sildenafil, EHNA (erythro-9-(2-hydroxyl-3-nonyl)adenine), zaprinast; or spiro bicyclic structures including bypyridines, amrinone; imidazolines, CI930; dihydropyridazinones, indolan, rolipram, SB207499; or fused biaryl structures including papaverine, dihydroquinilones, cilostamide, dipyridamole, vinpocetine and analogues thereof.

7 (currently amended) Library as claimed in ~~any of~~ Claims 1 ~~to 6~~ wherein J_{Lm} L J_{Tm} comprises a mono, di, tri, tetra, penta, or hexa amino, alkylthio, alkoxy, carboxylic acid, and combinations thereof including a mono, di or tri aminoalkylthio, amino alkoxy, alkoxy carboxylic acid or alkoxy amine, mono, di or tri amino menthane, amino ethane, thio ethane, ethane, amino acyl, polypeptide, or mono or polyether derivatives including diamine or dithio derivatives, mono or polyethylene glycol di or tri amine or thio;
or comprises a mono-, di-, tri- or tetra, penta or hexafunctional linear or branched or cyclic substituted or unsubstituted hydrocarbyl of formula –L.I-

$$J\,[\,A\,]\,q_L\,R_L\,[\,A'q_{L'}\,J'\,]_p\,A''q_{L''}\,J''$$

wherein each of J to J'' is a linking site or functionality as hereinbefore defined independently selected from a single or double bond, methylene, alkyne, alkene, NR, O, CONR, NRCO, S, CO, NCO, CHHal and P wherein R is H or C_{1-8} alkyl or cycloalkyl or forms part of a cyclic ring with N, Hal is any halogen selected from chlorine, iodine, bromine; and is present in any rational location in a group A to A'';
each of A to A '' is a group selected from –O-, -C(=O)-, C_{1-12} alkoxy, alkoyl, cycloalkyl, heterocyclic, alkyl, alkenyl, aryl, arylamide, arylamine, amino, thioalkyl, heteroaryl as hereinbefore defined and combinations thereof, optionally substituted by groups selected independently from C_{1-3} alkyl and C_{1-5} alkoxy;
each of q_L to q_L'' are independently-selected from 0 or 1 or indicates an oligomeric repeat and is from 2 to 30, or indicates a polymeric repeat unit and is from 31 up to 300.

R_L is a C, N or S atom or is a $CR_{L'}$, $NR_{L'}$, alkyl, cycloalkyl, heterocyclic, aryl heteroaryl, amine or thio moiety and provides for branching when p is 1 or 2; wherein $R_{L'}$ is H or C_{1-3} alkyl; and

p is as hereinbefore defined and is 0, 1 or 2.

8. (currently amended) Library as claimed in ~~any of~~ Claims 1 ~~to 7~~ wherein J_{Lm} L J_{Tm} is of formula
J Aq_L R_L J''
wherein each of J and J'' is amine or –O-, A is CH_2CH_2O, q_L is 1-30 or 31 to 300 and R_L is CH_2CH_2
or of formula
J Aq_L R_L(A'J') J''
wherein each of J, J' and J'' independently is amine, –O or a single bond, q_L is 1, 2 or 3 -30 or 31 to 300 and A is CH_2CH_2O or $HNCH_2CO$ or q_L is 1 and A is C(O) or $(CH_2)_{1-8}$ or q_L is 0, R_L is CH or CH_2CH, $q_{L'}$ is 0 or q_L' is 1 and A' is CH_2 and $q_{L''}$ is 0
preferably
$O(CH_2CH_2O)q_LCH_2CH_2NH$, $O(CH_2CH_2O)q_LCH_2CH(CH_2NH)NH$,

$OCH(CH_2NH)NH$, $-CH(CH_2NH)NH$, $-C(O)\ NH-$, $-(CH_2)_{1-8}-$ or $(-HNCH_2CO-)_{1-3}$ (= $-gly_{1-3}-$) -.

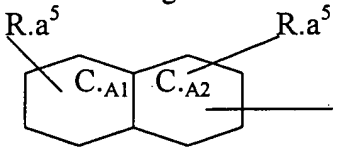
9. (currently amended) Library as claimed in ~~any of~~ Claims 1 ~~to 8~~ wherein each compound of formula I or I' comprises a moiety Lig and L as hereinbelow defined:
Wherein:
any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers
$Lig.a_m$ is suitably of the formula, in either of the following forms given, including any of its possible linking configurations or sites:

$Lig.a^1{}_m$

Wherein at least one or all of Ra^1 to Ra^4, X^1 and X^2 comprise a linking site or functionality J as hereinbefore defined
X^1 and X^2 are each independently selected from H, O, OR.a, NR.a, NHR.a;
X^1 and X^2 are each preferably O;
each of $R.a^1$, $R.a^2$, $R.a^3$ and $R.a^4$ independently is selected from H or C_{1-4} linear or branched alkyl optionally mono or multi hydroxy or halo substituted;

$R.a^4$ is selected from a heteroatom O, S or substituted or unsubstituted amine or saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo and cyano; including optionally substituted aryl, cycloalkyl, alkyl, ketone, (di)amine, (di)amide, alkoxy, cycloalkyl, carboxylic acid or optionally o-, m- or p- substituted phenyl wherein substituents include aryl, alkyl, cycloalkyl, heteroaryl or heteroalkyl, amine, amide, carboxyl, carbonyl or $R.a^4$ comprises cyclohexyl, cyclopentyl, ethoxy, $(CH_2)_2PhPh$, CH_2Ph, $CONH(CH_2)nCONH$, $CH_2CONH(CH_2)_2NH$, $CH_2PhNHCOCH_2$, $CH_2CH_2OCOCH_2$, succinimidyl ester, $NHCOCH_2$, $CH_2(CH_3)NCOCH_2$, $H_2N(CH_2)_2NHCOCH_2$, $H_2N(CH_2)_8NHCOCH_2$, $H_2NNHCOCH_2$, $CH_2CONH(CH_2)_2NHCOCH_2$, $HOPhCH_2N(CH_2CH_3.HOAc)(CH_2)_2NHCOCH_2$, heterocyclic-$(CH_2)_4CONH(CH_2)_2NHCOCH_2$ or heterocyclic-$NHCON(heterocyclic)COCH_2$;

or Lig.a is of the formula Lig.a^2-

Lig.a^2  R.a^6

wherein at least one or all of Ra^5 to Ra^6, or a cyclic C or heteroatom comprise a linking site or functionality J as hereinbefore defined, each of $C._{A1}$ and $C._{A2}$ is independently selected from C_{5-6} aryl, heteroaryl, cycloalkyl and heterocyclic, more preferably from phenyl, or aryl containing 1 or 2 ring heteroatoms, or heterocyclic containing 1 ring heteroatom and/or 1 ring –C=C- group;

Each of up to seven R.a^5 is a substituent of a ring carbon or a ring heteroatom and:

is independently selected from H, halo, hydroxy, thiol, amine, COOH, hydrazine, cyano, saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, and wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo =O or cyano; OCH_3, $CH_2Ph(OCH_3)_2$, $O(CH_2)_3CON(CH_3)$c.hex, $N(CH_2CH_2OH)_2$, c.hex, $COOCH_2CH_3$, CH_2CH_3;

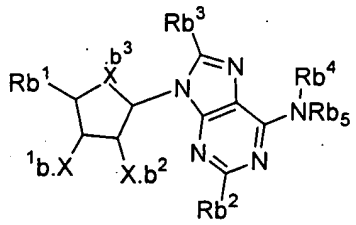
or any two or more of R.a^5 form a one, two or three ring fused cyclic structure, a fused 3 ring aryl, 5-heterocyclic or 6-heterocyclic structure having 4 ring atoms common with the fused bicyclic Lig.a^{2}structure;

and R.a^6 is a moiety as defined for R.a^5 above;

and L.a is as hereinbefore defined for L or J_L L J_T or L.I or subformulae as hereinbefore defined, or is a single bond, amino acid or amide including a peptide or polypeptide gly or gly_3, alkyl of formula $–(CH_2)_n$ where n is 3 to 8, optionally including one or more heteroatoms or unsaturated groups, including –O- or –S- or –CH=CH-:

Lig.b is suitably of the formula Lig.b including any of its possible linking configurations or sites:

Lig.b



wherein at least one or all of Rb^1 to Rb^5 or Xb^1 to Xb^3 comprise a linking site or functionality J as hereinbefore defined

ring substituents $X.b^1$ and $X.b^2$ are independently selected from hydrocarbon including alkyl or SR_X, $NR_{X.2}$ and OR_X wherein (each) R_X is selected from H, C_{1-5}alkyl, alkenyl;
ring heteroatom $X.b^3$ is selected from –S-, -O- and $–CH_2$-;

Rb^1 is selected from saturated or unsaturated, substituted or unsubstituted C_{1-4} aliphatic, or C_{1-3} alicyclic optionally including one or more heteroatoms N, O, S, P, wherein substituent(s) are selected from one or more cycloalkyl, heterocyclic, hydroxy, oxo, halo, amine; or $R.b^1$ comprises a carbonyl substituted by H, alkyl or a linear or cyclic primary, secondary or tertiary amine, substituted C_{1-3} alkyl, cycloalkyl or amide, cyclopropyl, or $CONHC_{1-3}$alkyl including CONHEt or CH_2OH

and each of $R.b^2$ and $R.b^3$ is selected from H, halo, hydroxy, thiol, amine, COOH, CHO, hydrazine, cyano or saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano, preferably from H, halo or hydroxy;

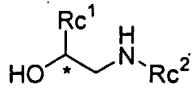
Rb^4 is H;

Rb^5 is H or alkyl

L.b comprises a linking site or functionality J as hereinbefore defined; and is as hereinbefore defined for L or its subformulae, more preferably is saturated and unsaturated substituted or unsubstituted C_{1-12} aliphatic or C_{1-24} aromatic as defined for L optionally including one or more heteroatoms O, S or N, cyclic or heterocyclic groups, or is of formula L.I or its subformulae as hereinbefore defined, or is (CH_2)m wherein m is 2 to 12, or is $(Ph\text{-}CH_2CONH)_2$ $(CH_2)_2$;

Lig.c is of the formula Lig.c including any of its possible linking configurations or sites:

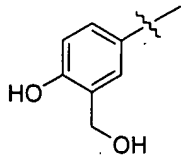
Lig.c $HOC^*(R.c^1)CH_2NH\text{-}R.c^2$



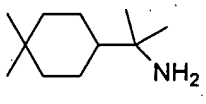
where at least one or all of Rc^1 to Rc^2 or OH, or a chain C or N comprise a linking site or functionality J as hereinbefore defined

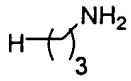
* indicates an optically active centre and

wherein $R.c^1$ is C_{6-14} aryl optionally including one or more heteroatoms selected from H, O, optionally substituted by OH, Hal, NH_2, NHC_{1-3}alkyl, sulphonamide, oxoamine or (-$CONH_2$), or is mono, di or tri substituted phenyl or quinoline wherein substituents include OH, Cl or NH_2, or is m-CH_2OH, p-OH phenyl, m-,p-dihydroxy phenol or m-,m-dihydroxyphenol, m-,m-diCl, p-NH_2 phenol, p-OH, m-$CONH_2$ phenol or 5-OH, 8-quinoline,



$R.c^2$ is selected from saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}20}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any optionally substituted $C_{1\text{-}12}$ aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano and combinations thereof; or $R.c^2$ is selected from $C_{1\text{-}6}$ branched or straight chain aliphatic, $C_{6\text{-}10}$ araliphatic optionally substituted by OH and optionally including heteroatoms selected from N,O, optionally including an ether O, and is selected from $-(CH_2)_6OCH((CH_2)_3Ph)$, $CHCH_3(CH_2)_2Ph$, $CHCH_3CH_2PhOH$, $C(CH_3)_2CH_2Ph$ or from the structures:

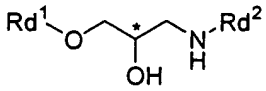




L.c is present as $R.c^2$ or comprises a linking site or functionality J as hereinbefore defined, and is as hereinbefore defined for L, formula L.I or its subformulae as hereinbefore defined, or is selected from $C_{1\text{-}12}$ alkyl, amide;

Lig.d is of the formula Lig.d including any of its possible linking configurations or sites:

Lig.d $R.d^1\ OCH_2C^*HOHCH_2NH\text{-}R.d^2$

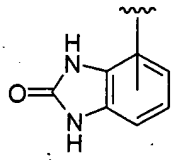
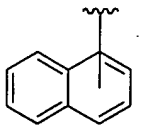
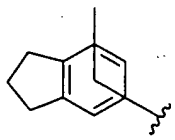
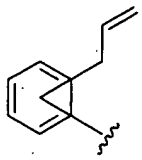
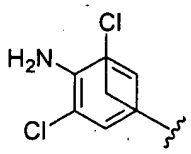


where at least one or all of Rd^1 to Rd^2 or OH, a chain C or N comprise a linking site or functionality J as hereinbefore defined

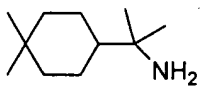
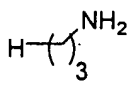
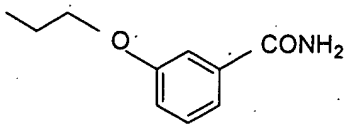
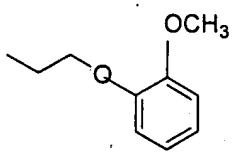
* indicates an optically active centre

wherein $R.d^1$ is saturated or unsaturated, substituted or unsubstituted $C_{1\text{-}20}$ branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any $C_{1\text{-}12}$ aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano; or $R.d^1$ is substituted or unsubstituted $C_{1\text{-}24}$ aralkyl or heteroaralkyl, including

single ring and fused ring systems with (hetero)aryl or cycloalkyl rings, wherein optional substituents include C_{1-6} alkyl, alkoxy, ether, carbonyl, alkenyl, amine, amide each optionally carbonyl, amide, halo or OH substituted, or halo or OH, amine, amide, carbonyl, ketone, ether substituted phenyl or naphthyl, mono-, di-, tri- or tetra substituted mono or polycyclic fused aryl or cycloaryl or heterocycloaryl including phenyl, carbazole or structures shown below or spiro ring systems, mono-, di-, tri- or tetra alkoxyalkyl, alkoxyalkoxyalkyl or CF_3 substituted phenyl or unsubstituted or monosubstituted naphthalene or 5,6 ring systems:

$R.d^2$ is substituted or unsubstituted amine, saturated or unsaturated, substituted or unsubstituted C_{1-12} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P; wherein optional substituents are selected from any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo or cyano, more preferably amine, C_{1-6} branched or straight chain alkyl optionally including ether O, and optionally substituted by C_{6-10} aryl, or of the formula:

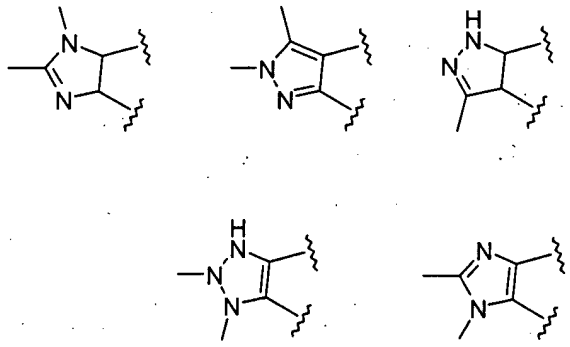
L.d may be present as $R.d^2$ or may comprise a linking site or functionality J as hereinbefore defined and is as hereinbefore defined for L and its subformulae , formula L.I and its subformulae as hereinbefore defined, or is a single bond or is as hereinbefore defined for L.a;

Lig.e comprises a cell permeant moiety or is associated with a cell permeant L or Fl moiety or is of the formula , in either of the following forms given including any of its possible linking configurations or sites:

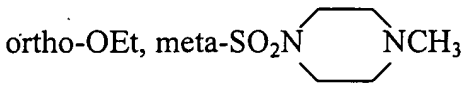
Lig.e^1

wherein at least one or all of Re^1 to Re^4, X and a ring C or N comprise a linking site or functionality J as hereinbefore defined

h is selected from



each optionally substituted by $R.e^3$ – $R.e^4$ wherein $R.e^1$ – $R.e^4$ are as $R.a^1$ – $R.a^4$ defined above or in which $R.e^3$ is C_{5-9} linear or branched alkyl, optionally mono or multi hydroxy or halo substituted or is aryl optionally substituted by alkoxy or sulfonyl,

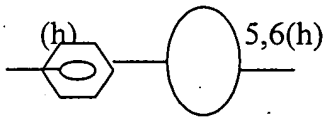


each X is independently selected from H, O, $-OR.e^2$, N, HN, $NR.e^5$, $HR.e^6$, and aryl optionally substituted by ether; or X is aryl optionally alkyl or alkoxy substituted or is Ph-ortho-$OCH_2CH_2CH_3$;

and where $R.e^5$ is as defined above for $R.e^1$ above or forms a fused cyclic ring together with the adjacent ring N atom, or 1 or 2 fused 5 membered cyclic rings;

and R.e^6 is as defined above for R.e^1 above or is selected from optionally substituted phenyl wherein optional substituents include ether, o-ethoxy or o-propoxy, alkyl or OH, sulphonyl or carbonyl substituted by heterocyclic, or cyclic C_{5-8} alkyl, piperazinyl or sulphonyl;

or Lig.e is of the formula Lig.e^2

Lig.e^2 

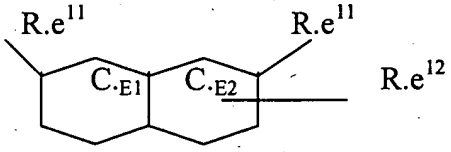
wherein at least one or all free ring atom or their substituents comprise a linking site or functionality J as hereinbefore defined

each spiro ring optionally comprises zero or one or more heteroatoms h

or (h)  comprises zero or 1 N heteroatom and  5,6(h) comprises zero, 1 or 2 N heteroatoms and is unsaturated or comprises one or two –C=C- or -C=N- groups;

and wherein each ring is optionally substituted by one or more oxo, CO, COOH, C_{1-6} alkyl or linear or cyclic alkoxy optionally substituted by one or more oxo, CO, COOH, CN, or C_{1-6} alicyclic or amine groups, amine or one or more spiro or fused heterocycles;

or Lig.e is of the formula Lig.e^3

Lig.e^3 

wherein at least one or all of Re^{11} to Re^{12}, or a ring C or heteroatom or ring substituent comprise a linking site or functionality J as hereinbefore defined

each of C.$_{E1}$ and C.$_{E2}$ is independently selected from C_{5-6} aryl, heteroaryl, cyloalkyl and heterocyclic, including phenyl, or aryl containing 1 or 2 ring heteroatoms, or heterocyclic containing 1 ring heteroatom and/or 1 ring –C=C- group;

each of up to seven R.e^{11} is a substituent of a ring carbon or a ring heteroatom and:

is independently selected from saturated or unsaturated, substituted or unsubstituted C_{1-20} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, and wherein optional substituents are selected from

any C_{1-12} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo =O, or cyano, OCH_3, $CH_2Ph(OCH_3)_2$, $O(CH_2)_3CON(CH_3)$c.hex, $N(CH_2CH_2OH)_2$, c.hex, $COOCH_2CH_3$, CH_2CH_3;

or any two or more of R.e[11] form a one, two or three ring fused cyclic structure, a fused 3 ring aryl, 5-heterocyclic or 6-heterocyclic structure having 4 ring atoms common with the fused bicyclic Lig.e[3] structure;

and R.e[12] is a moiety as defined for R.e[11] above;

L.e comprises a linking site or functionality J as hereinbefore defined and is suitably as hereinbefore defined for L.a.

10. (currently amended) Library as hereinbefore defined in ~~any of~~ Claims 1 ~~to 9~~ wherein Fl is selected from dyes in particular including fluorescein, fluorescein derivatives including FITC, and fluorescein-like molecules including Oregon Green™ and its derivatives, Texas red™, 7-nitrobenz-2-oxa-1,3-diazole (NBD) and derivatives thereof, coumarin and derivatives, naphthalene including derivatives of dansyl chloride or its analogues or derivatives, Cascade Blue™, EvoBlue and fluorescent derivatives thereof, pyrenes and pyridyloxazole derivatives, the cyanine dyes, the dyomics (DY dyes and ATTO dyes) and fluorescent derivatives thereof, the Alexafluor dyes and derivatives, BDI dyes including the commercially available Bodipy™ dyes, erythosin, eosin, pyrenes, anthracenes, acridines, fluorescent phycobiliproteins and their conjugates and fluoresceinated microbeads, Rhodamine and fluorescent derivatives thereof including Rhodamine Green™ including the tetramethylrhodamines, X-rhodamines and Texas Red derivatives, and Rhodol Green™, coupled to amine groups using the isocyanate, succinimidyl ester or dichlorotriazinyl-reactive groups.

11 (original) Library as claimed in Claim 10 wherein Fl is of formula $J_T - t - Fl$ and comprises a BODIPY ™ structure characterised by a dipyrromethene boron difluoride core, optionally modified by one or two fused rings, optionally substituted by one or several substituents selected from alkyl, alkoxy, aryl or heterocyclic, wherein one substituent –t- is adapted for linking as hereinbefore defined to a ligand precursor as hereinbefore defined, wherein the substituent –t- comprises a proximal unsaturated or aryl moiety, comprising a medial short, medium or long chain alkynyl or cycloalkyl moiety and comprising a moiety derived from linking via a reactive group as hereinbefore defined or selected from carboxyl, sulphonate or as a heteroatom O or S or methylene derived from linking at an alkylhalide including methylbromide, haloacetamide or sulphonate ester electrophilic group.

12. (currently amended) Library as claimed in ~~any of~~ Claims 1 ~~to 11~~ comprising a plurality of compounds of the formula

Lig J_L L J_T Fl

wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers

wherein Fl is selected from dyes in particular including fluorescein, fluorescein derivatives including FITC, and fluorescein-like molecules including Oregon Green™ and its derivatives, Texas red™, 7-nitrobenz-2-oxa-1,3-diazole (NBD) and derivatives thereof, coumarin and derivatives, naphthalene including derivatives of dansyl

chloride or its analogues or derivatives, Cascade Blue™, EvoBlue and fluorescent derivatives thereof, pyrenes and pyridyloxazole derivatives, the cyanine dyes, the dyomics (DY dyes and ATTO dyes) and fluorescent derivatives thereof, the Alexafluor dyes and derivatives, BDI dyes including the commercially available Bodipy™ dyes, erythosin, eosin, pyrenes, anthracenes, acridines, fluorescent phycobiliproteins and their conjugates and fluoresceinated microbeads, Rhodamine and fluorescent derivatives thereof including Rhodamine Green™ including the tetramethylrhodamines, X-rhodamines and Texas Red derivatives, and Rhodol Green™, coupled to amine groups using the isocyanate, succinimidyl ester or dichlorotriazinyl-reactive groups,
and
wherein Lig J_L L J_T is selected from:
xanthine like structures
adenosine like structures;
ethanolamine like structures; and
oxypropanolamine like structures; wherein
linking functionality J_T is amine; and
wherein linker L is selected from branched and straight chain C_{1-50} alkyl, C_{6-50} cycloalkyl or aryl and combinations thereof optionally comprising one or more heteroatoms O and optionally substituted by C_{1-12} aliphatic, or for xanthine like structures L is also selected from a single bond.

13. (currently amended) Process for the preparation of a library as claimed in ~~any of~~ Claims 1 ~~to 12~~ which is a combinatorial process; and comprises the reaction of one or more ligand precursors of formula IV and/or IV'
IV $(LigJ_L)_m - L - Y_{Lm}$
IV' $Lig\ Y_{Ligm}$
comprising one or more or different reactive groups Y_L or Y_{Lig} forming a linking functionality J, J_L or J_T as hereinbefore defined
with one or more of a plurality of analytical tagging substrates of formula V and/or V'

V $Y_{Tm}\ Tag$
V' $Y_{Tm}\ L\ (J_T Tag)_m$
comprising one or more or different reactive groups Y_T forming a linking functionality J or J_T as hereinbefore defined
and optionally one or more linking species VI or VI' or VI''
VI $Y_{Lm} L\ Y_{Lm}$
wherein Lig, J, L, J_T and Tag and each m is independently as hereinbefore defined
wherein the or each compound of formula IV or IV' is capable of reaction with the or each compound of formula V or V', optionally via the or each species VI or VI' or VI'' to form a plurality of compounds of formula I as hereinbefore defined;
wherein linking is at same or different reactive sites in different compounds as hereinbefore defined.

14 (currently amended) Process for the preparation of a compound of formula I as hereinbefore defined in ~~any of~~ Claims 1 ~~to 12~~ comprising the reaction of a compound of formula IV or IV' and a compound of formula V or V' and optionally additionally VI, as hereinbefore defined, by reacting the unprotected primary alkyl amine group of a compound of formula IV with a compound of formula V comprising

a reactive succinimidyl ester group in solvent at ambient temperature without the need for subsequent deprotection.

15 (currently amended) Process for the preparation of a compound of formula IV as hereinbefore defined in Claim 13 ~~or 14~~ comprising: obtaining where commercially available or preparing the ligand precursor Lig, by routes as known in the art, and reacting with linker precursor VI'', if required, or components thereof, and/or generating one or more reactive sites Y or Y_{Lig} or Y_L, by a method selected from:
a), e) ring closure of 5,6-diamino-1,3-dialkyl uracil with the appropriate substituted aldehyde under acid conditions with ferric chloride,
b) reacting Lig.b- comprising a protected inosine derivative with chlorinating agent and linking the chloro derivative with the amine group of a suitably protected amine reactive linker H–L-P_L wherein P_L comprises *N*-benzyloxycarbonyl- to form Lig.b -L-P_L and removing P_L to generate Lig.b –L.b; preferably $R.b^1$ comprises a OH terminating group and protected inosine comprises Acyl protecting groups or $R.b^1$ comprises a stable group such as amine or amide and protected inosine comprises 2,2-dimethoxypropane protecting group; preferably the protected inosine is reacted with oxidising agent and protected alkylamine which is an *N*-alkylcarboxamide with removal of amine protecting group to generate a reactive ligand;
c), d) reacting *p*-hydroxybenzaldehyde with formaldehyde under acid catalysis and protection of the resulting 4-hydroxy-3-hydroxymethylbenzaldehyde with dimethoxypropane to generate the resulting acetonide, converting the Benzaldehyde to its corresponding epoxide and ring opening with a suitably protected linker such as Boc-L.c-H supplies Lig_m-L-P_L, finally, deprotection under acid conditions supplies Lig.cLc or Lig.dLd for coupling to an appropriate tag.

16 (currently amended) Method for selecting a compound of formula I from a library as claimed in ~~any of~~ Claims 1 ~~to 12~~ comprising the rational design of a library of compounds of formula I as hereinbefore defined using the process ~~as hereinbefore defined in Claim 13Process~~ for the preparation of a library as claimed in ~~any of~~ Claims 1 ~~to 12~~ which is a combinatorial process; and comprises the reaction of one or more ligand precursors of formula IV and/or IV'

IV $(LigJ_L)_m$ –L –Y_{Lm}

IV' Lig Y_{Ligm}

comprising one or more or different reactive groups Y_L or Y_{Lig} forming a linking functionality J, J_L or J_T as hereinbefore defined
with one or more of a plurality of analytical tagging substrates of formula V and/or V'

V Y_{Tm} Tag

V' Y_{Tm} L $(J_T Tag)_m$

comprising one or more or different reactive groups Y_T forming a linking functionality J or J_T as hereinbefore defined
and optionally one or more linking species VI or VI' or VI''

VI Y_{Lm}L Y_{Lm}

wherein Lig, J, L, J_T and Tag and each m is independently as hereinbefore defined
wherein the or each compound of formula IV or IV' is capable of reaction with the or each compound of formula V or V', optionally via the or each species VI or VI' or VI'' to form a plurality of compounds of formula I as hereinbefore defined;

wherein linking is at same or different reactive sites in different compounds as hereinbefore defined, determining pharmacology for a plurality of or all compounds in the library and selecting a compound exhibiting desired pharmacology.

17 (original) Method as claimed in Claim 16 which comprises preparing a preliminary library of compounds, conducting screens to assess binding or inhibition, selecting a compound identified in the screen as having beneficial properties, and modifying or functionalising by nature of moieties or linking location of linking on the basis of the indications from the screen to prepare an optimised library, wherein the molecular pharmacology and photochemistry from the screen feedback into the design of the library.

18. (currently amended) A compound of formula I

$(Lig\ J_L)_m\ L\ (J_T\ Tag)_m\ (J_T\ L\ (J_L\ Lig)_m)_p$

or salt thereof as hereinbefore defined in Claim 1 ~~or 2 or dependent claims~~ wherein $JL_m\ L\ T_{Tm}$ is ~~as hereinbefore defined in Claim 8~~ is of formula

$J\ Aq_L\ R_L\ J''$

wherein each of J and J'' is amine or –O-, A is CH_2CH_2O, q_L is 1-30 or 31 to 300 and R_L is CH_2CH_2

or of formula

$J\ Aq_L\ R_L(A'J')\ J''$

wherein each of J, J' and J'' independently is amine, –O or a single bond, q_L is 1, 2 or 3 -30 or 31 to 300 and A is CH_2CH_2O or $HNCH_2CO$ or q_L is 1 and A is C(O) or $(CH_2)_{1-8}$ or q_L is 0, R_L is CH or CH_2CH, q_L' is 0 or q_L' is 1 and A' is CH_2 and q_L'' is 0

preferably

$O(CH_2CH_2O)q_LCH_2CH_2NH$, $O(CH_2CH_2O)q_LCH_2CH(CH_2NH)NH$, $OCH(CH_2NH)NH$, $-CH(CH_2NH)NH$, -C(O) NH-, $-(CH_2)_{1-8}-$ or $(-HNCH_2CO-)_{1-3}$ (= $-gly_{1-3}-$) - and wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers.

19. (currently amended) A compound of formula II or III as hereinbefore defined in Claim ~~4 or dependent claims~~

II $(LigJ_L)_m\ L\ J_T\ TagJ_T\ L\ (J_L\ Lig)_m$ where each m is as hereinbefore defined and is preferably 1 or 2, more preferably 1

III $(LigJ_L)_m\ L\ (J_TTag)_m$ wherein each m is as hereinbefore defined and is preferably 1 and/or 2, more preferably

$Lig\ J_L - L - J_L\ Tag$ and/or

$Lig\ J_L - L - J_T\ Tag$ and/or $Lig\ J_L - L - J_T\ Tag$

$\diagdown J_L\ Lig$ $\diagdown J_T\ Tag$

as hereinbefore defined in Claim 4 and wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers.

20. (currently amended) A compound according to Claim 18 ~~or 19~~, wherein Lig comprises a GPCR ligand, an inhibitor of an intracellular enzyme or a substrate or inhibitor of a drug transporter or Fl is a fluorophore entity, with the proviso that when Lig is CGP12177 and L is 1,1,4,4-tetramethyl butylamine $C(CH_3)_2(CH_2)_2$-$C(CH_3)_2NH$-, Fl is not BODIPY® FL, or when L is $C(CH_3)_2(CH_2)_2C(CH_3)_2NHCSNH$ – then Fl is not FITC, eosin or erythrosin

characterised in that the or each Fl is selected from a red, near ir or blue absorbing dye or from BODIPY® 630/650 or BODIPY® 630/650 X~~as hereinbefore defined in Claims 2, 6, 10 or 11~~.

21 (currently amended) A compound of the formula I or I' as hereinbefore defined in ~~any of~~ Claims 10 ~~to 12 or 18 to 20~~ selected from formulae Lig.a_m L.a-Fl.a_n to Lig.e_m L.eFl.e_n as hereinbefore defined
with the proviso that:

a) when Lig is XAC ie in Lig.a when each of R.a^1 and R.a^2 is propyl, R.a^3 is H and R.a^4 is –Ph-$OCH_2CONH(CH_2)_2NH$-, and L is a single bond or L is gly and n=3 or L is NCS, Fl is not fluorescein; or
when Lig is XAC and L is a single bond or NCS, Fl is not fluorescein or NBD;

b) when Lig is adenosine Fl is not Fmoc (CA 134:204756); or
when Lig is ADAC , ie R.b^1 is CH_2OH, R.b^2 and R.b^3 are H and L is –(Ph-$CH_2CONH)_2(CH_2)_2$- or L is a single bond, Fl is not fluorescein, NBD or Rhodamine; or
when Lig is NECA (incorporating the moiety –(CH_2)m) ie R.b^2 and R.b^3 are H and L is a single bond, or is –(CH_2)m when m is 2,4,6,8 or 10 then Fl is not NBD, or when m is 3,4,6,8,10 or 12 then Fl is not dansyl; or
when Lig is N^6-[2-(4-aminophenyl)ethyl]adenosine and L is $(CH_2)_2$PhNH, Fl is not FITC (CA 131:56155 (8))

d) when Lig is CGP12177 and L (R.d^2) is mono amine menthane, Fl is not BODIPY® TMR; or
when Lig is CGP12177 and L is 1,1,4,4-tetramethyl butylamine, i.e $C(CH_3)_2(CH_2)_2C(CH_3)_2NH$- Fl is not BODIPY® FL, or when L is $C(CH_3)_2(CH_2)_2C(CH_3)_2NHCSNH$- then Fl is not FITC, eosin or erythosin; or when L is monoamine menthane, Fl is not FITC (CA 131:56155 (4)); or
when Lig is CGP12177 and L is a single bond, Fl is not NBD; or
when Lig is alprenolol i.e o-prop-2-enyl phenyl and L is –$C(CH_3)_2$- or a single bond, Fl is not NBD;
and a) – e) when L is a single bond, Fl is not BODIPY FL;
optionally additionally
a) when Lig is XAC ie in Lig.a when each of R.a^1 and R.a^2 is propyl, R.a^3 is H and R.a^4 is –Ph-$OCH_2CONH(CH_2)_2NH$-, and L is a single bond Fl is not BODIPY ™ 630/650 X; or
b) when Lig is ABEA, ie m is 4 and L is a single bond Fl is not BODIPY™ 630/650 X.

22. (currently amended) A compound of the formula

Lig J_L L J_T Fl as defined in ~~any of~~ claims 1 ~~to 11 or 18 to 21~~
wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers
wherein Fl is a fluorophore as hereinbefore defined ~~in claim 10 or 11~~ and is selected from dyes in particular including fluorescein, fluorescein derivatives including FITC, and fluorescein-like molecules including Oregon Green™ and its derivatives, Texas red™, 7-nitrobenz-2-oxa-1,3-diazole (NBD) and derivatives thereof, coumarin and derivatives, naphthalene including derivatives of dansyl chloride or its analogues or derivatives, Cascade Blue™, EvoBlue and fluorescent derivatives thereof, pyrenes and pyridyloxazole derivatives, the cyanine dyes, the dyomics (DY dyes and ATTO

dyes) and fluorescent derivatives thereof, the Alexafluor dyes and derivatives, BDI dyes including the commercially available Bodipy™ dyes, erythosin, eosin, pyrenes, anthracenes, acridines, fluorescent phycobiliproteins and their conjugates and fluoresceinated microbeads, Rhodamine and fluorescent derivatives thereof including Rhodamine Green™ including the tetramethylrhodamines, X-rhodamines and Texas Red derivatives, and Rhodol Green™, coupled to amine groups using the isocyanate, succinimidyl ester or dichlorotriazinyl-reactive groups, and
wherein Lig J_L L J_T is selected from:
xanthine like structures
adenosine like structures;
ethanolamine like structures; and
oxypropanolamine like structures; wherein
linking functionality J_T is amine; and
wherein linker L is selected from branched and straight chain $C_{1\text{-}50}$ alkyl, $C_{6\text{-}50}$ cycloalkyl or aryl and combinations thereof optionally comprising one or more heteroatoms O and optionally substituted by $C_{1\text{-}12}$ aliphatic, or for xanthine like structures L is also selected from a single bond,

with the proviso that when Lig is XAC ie in Lig.a when each of R.a^1 and R.a^2 is propyl, R.a^3 is H and R.a^4 is –Ph-$OCH_2CONH(CH_2)_2NH$-, and L is a single bond Fl is not BODIPY ™ 630/650 X; or
b) when Lig is ABEA, ie m is 4 and L is a single bond Fl is not BODIPY™ 630/650 X. ~~the compound is not a compound excluded in Claim 21~~.

23 (currently amended) A kit comprising a Compound of formula I or I' as hereinbefore defined in ~~any of~~ Claims 1 ~~or 2 to 12, or 18 to 22~~ associated with information relating to its pharmacological properties in the form of Spectral Properties given as Excitation Max and Emission Max, Fluorescence Lifetime and Emission quantum yield and Pharmacology defined in terms of cells expressing a GPCR receptor as hereinbefore defined or expressing an intracellular cyclic nucleotide phosphodiesterase, or a drug transporter as hereinbefore defined and given as the Inhibition or Antagonism of receptor binding or of receptor functionality together with a value for the Inhibition (pK_B) or Antagonism (pK_I) binding constants, and optionally together with fluorescent images of the pharmacological binding in single living cells illustrating the defined inhibition or antagonism, preferably the pharmacological properties are given as EC_{50} values for agonist stimulated – or pK_i values for antagonism of agonist stimulated second messenger generation, or substrate K_m values or antagonist K_i values for stimulation or inhibition of intracellular enzymes or drug transporters.

24 (currently amended) Compound of formula IV or IV' or library thereof as hereinbefore defined in Claim 13 useful for linking to any suitable tag of formula V or V' as hereinbefore defined in Claim 13,
wherein the linker moiety ~~is of formula as defined in Claim 8~~ J_{Lm} L J_{Tm} is of formula
J Aq_L R_L J''
wherein each of J and J'' is amine or –O-, A is CH_2CH_2O, q_L is 1-30 or 31 to 300 and R_L is CH_2CH_2
or of formula
J Aq_L R_L(A'J') J''

wherein each of J, J' and J'' independently is amine, –O or a single bond, q_L is 1, 2 or 3 -30 or 31 to 300 and A is CH_2CH_2O or $HNCH_2CO$ or q_L is 1 and A is C(O) or $(CH_2)_{1-8}$ or q_L is 0, R_L is CH or CH_2CH, q_L' is 0 or q_L' is 1 and A' is CH_2 and q_L'' is 0 preferably
$O(CH_2CH_2O)q_LCH_2CH_2NH$, $O(CH_2CH_2O)q_LCH_2CH(CH_2NH)NH$, $OCH(CH_2NH)NH$, $-CH(CH_2NH)NH$, -C(O) NH-, $-(CH_2)_{1-8}-$ or $(-HNCH_2CO-)_{1-3}$ (= $-gly_{1-3}-$) -.

25 (currently amended) Fluorophore linker of formula V' or library thereof as hereinbefore defined in ~~any of~~ Claims 13 ~~to 14~~ wherein the linker moiety ~~is of formula as defined in Claim 8~~ J_{Lm} L J_{Tm} is of formula
J Aq_L R_L J''
wherein each of J and J'' is amine or –O-, A is CH_2CH_2O, q_L is 1-30 or 31 to 300 and R_L is CH_2CH_2
or of formula
J Aq_L R_L(A'J') J''
wherein each of J, J' and J'' independently is amine, –O or a single bond, q_L is 1, 2 or 3 -30 or 31 to 300 and A is CH_2CH_2O or $HNCH_2CO$ or q_L is 1 and A is C(O) or $(CH_2)_{1-8}$ or q_L is 0, R_L is CH or CH_2CH, q_L' is 0 or q_L' is 1 and A' is CH_2 and q_L'' is 0 preferably
$O(CH_2CH_2O)q_LCH_2CH_2NH$, $O(CH_2CH_2O)q_LCH_2CH(CH_2NH)NH$, $OCH(CH_2NH)NH$, $-CH(CH_2NH)NH$, -C(O) NH-, $-(CH_2)_{1-8}-$ or $(-HNCH_2CO-)_{1-3}$ (= $-gly_{1-3}-$) -.

26 (currently amended) Kit comprising ligand precursors, linker precursors and tag precursors of formulae IV, IV', V, V' and/or VI as hereinbefore defined in ~~any of~~ Claims 13 ~~to 14~~ for preparing a library of compounds of formula I ~~as hereinbefore defined in any of Claims 1 to 12~~ defined as (Lig $J_L)_m$ L (J_T Tag) $_m$ (J_T L (J_L Lig)$_m$)$_p$ and salts thereof wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers
comprising one or a plurality of same or different ligand moieties Lig each linked to one or a plurality of same or different tag moieties Tag via same or different linker moieties L and same or different linking site or linking functionality J_T and J_L
wherein Lig comprises a GPCR ligand, an inhibitor of an intracellular enzyme or a substrate or inhibitor of a drug transporter;

L	is selected from a double bond, -O-, -S-, amine, COO-, amide, -NN- hydrazine; and saturated or unsaturated, substituted or unsubstituted C_{1-600} branched or straight chain aliphatic, aromatic, alicyclic and combinations thereof, any of which may comprise one or more heteroatoms selected from N, O, S, P, wherein optional substituents are selected from any C_{1-20} aliphatic, aromatic or alicyclic substituents any of which may comprise one or more heteroatoms as hereinbefore defined, hydroxy, thiol, halo, amine, hydrazine, oxo, cyano and carbonyl and combinations thereof, and L may be monomeric, oligomeric having oligomeric repeat of 2 to 30 or polymeric having polymeric repeat in excess of 30 up to 300;
Tag	is any tagging substrate;
m	are each independently selected from a whole number integer from 1 to 3;
p	is 0 to 3

wherein one or more of each -Tag in one or more or each library compound is a fluorophore entity -Fl, whereby the library comprises compounds of which one or more or all of which are of formula I'

$(Lig J_L)_m$ L $(J_T Fl)_m$ $(J_T L (J_L Lig)_m)_p$

characterised in that linking is at same or different linking sites in compounds comprising different Lig, J_L, L J_T and/or – Tag and is at different linking sites in compounds comprising same Lig, J_L, L J_T and/or – Tag

with the proviso that when Lig is CGP12177 and L is 1,1,4,4-tetramethyl butylamine $C(CH_3)_2(CH_2)_2C(CH_3)_2NH$-, Fl is not BODIPY® FL, or when L is $C(CH_3)_2(CH_2)_2$-$C(CH_3)_2NHCSNH$ – then Fl is not FITC, eosin or erythrosin.

27 (currently amended) A library of fluorescent ligands of formula I or I' or a kit comprising a compound thereof as hereinbefore defined in ~~any of~~ Claims 1 ~~or 2 to 12, or 18 to 23~~ for visualising receptors or receptor binding, assessing pharmacological properties of the fluorescent ligand, in high throughput screening of novel chemical entities that bind to the target receptor, in inhibiting an intracellular enzyme or inhibiting a drug transporter or a substrate of a drug transporter, in studying drug transport or drugs suitable for transport or in distinguishing healthy or diseased tissue.

28 (currently amended) A library of fluorescent ligands of formula I or I' or a kit comprising a compound thereof thereof as hereinbefore defined in ~~any of~~ Claims ~~1 or 2 to 12, 18 to 23~~ for use in a method for receptor binding or inhibition, intracellular enzyme inhibition or drug transport or inhibition and visualisation comprising contacting a library or a compound thereof as defined in ~~any of~~ Claims 1 ~~or 2 to 12 or 18 to 23~~ with a sample comprising live cell material comprising GPCRs, intracellular enzymes or drug transporters in manner to facilitate binding or inhibition thereof or transport thereby, and detecting changes in fluorescence or location thereof.

29. (original) A library of fluorescent ligands of formula I or I' or a kit comprising a compound thereof for use as claimed in Claim 28 wherein the library or compound thereof is a fluorescent ligand(s) which has affinity such that it binds permanently, semi-permanently or transiently and remains bound when unbound ligand is washed away.

30. (currently amended) A library of fluorescent ligands of formula I or I' or a kit comprising a compound thereof for use as claimed in Claim 28 ~~or 29~~ wherein detecting a change in fluorescence is by means of confocal microscopy or fluorescence correlation spectroscopy.

31. (currently amended) A library of fluorescent ligands of formula I or I' or a kit comprising a compound thereof for use as claimed in ~~any of~~ claims 28 ~~to 30~~ wherein the library or compound thereof comprises fluorescent ligand agonist(s) which maintain binding affinity and functional activity.

32 (currently amended) A kit comprising a library or a compound of formula I or I' as claimed in ~~any of~~ Claims 1 ~~or 2 to 12 or 18 to 23~~ and a target therefor provided as cell derived material selected from a cell line, expressing a GPCR, intracellular enzyme or drug transporter, membrane containing these proteins derived from such a

cell line, solubilised receptor, enzyme or drug transporter or GPCR array from that cell line.

33 (original) Kit as claimed in Claim 32 wherein the cell derived material is provided in one of three forms: (1) from cells expressing a green fluorescent protein tagged receptor, intracellular enzyme or drug transporter; (2) from cells expressing an epitope tag for a commercially available fluorescent antibody or (3) a wild-type protein for which a specific fluorescent antibody is also provided.

34. (currently amended) A library as hereinbefore defined ~~in any of the preceding claims~~ in claim 33 comprising a plurality of defined and characterised ligands having verified properties corresponding to those of the non-tagged ligand.

35. (currently amended) A library as hereinbefore defined in ~~any of the preceding claims~~ claim 34 comprising tagged ligands designed from reaction of reactive precursor ligands and reactive fluorophores having reactive site chemical functionality suited for reaction with associated reagents, for site specific reaction and linking, wherein the library design is the result of extensive pharmacological investigation of all or many of the possible linking sites and the resulting pharmacological characteristics and selection of one or more linking combinations which provide favorable binding, inhibition or transport characteristics.

36. (currently amended) A library or compound as hereinbefore defined in ~~any of the preceding claims~~ claim 35 wherein the or each Fl is selected from any red, near ir or blue absorbing dye or from BODIPY® 630/650 or BODIPY® 630/650 X.

37. (currently amended) Library as claimed in Claim 12 comprising a plurality of compounds of the formula

Lig J_L L J_T Fl

wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers

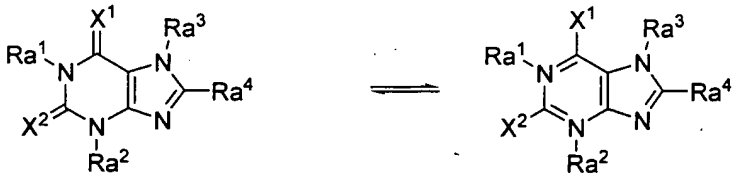
wherein Fl is selected from dyes in particular including fluorescein, fluorescein derivatives including FITC, and fluorescein-like molecules including Oregon Green™ and its derivatives, Texas red™, 7-nitrobenz-2-oxa-1,3-diazole (NBD) and derivatives thereof, coumarin and derivatives, naphthalene including derivatives of dansyl chloride or its analogues or derivatives, Cascade Blue™, EvoBlue and fluorescent derivatives thereof, pyrenes and pyridyloxazole derivatives, the cyanine dyes, the dyomics (DY dyes and ATTO dyes) and fluorescent derivatives thereof, the Alexafluor dyes and derivatives, BDI dyes including the commercially available Bodipy™ dyes, erythosin, eosin, pyrenes, anthracenes, acridines, fluorescent phycobiliproteins and their conjugates and fluoresceinated microbeads, Rhodamine and fluorescent derivatives thereof including Rhodamine Green™ including the tetramethylrhodamines, X-rhodamines and Texas Red derivatives, and Rhodol Green™, coupled to amine groups using the isocyanate, succinimidyl ester or dichlorotriazinyl-reactive groups,

and

wherein Lig J_L L J_T is selected from the formulae Lig.a, Lig.b, Lig.c and Lig.d wherein:

Lig.a comprises linking functionality J_L which is amine, and is of the formula, in either of the following forms given:

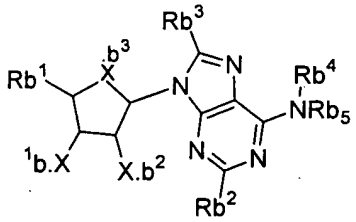
Lig.a $^{1}{}_{m}$



wherein Ra^4 comprises linking functionality J_L and J_T which is amine;
X^1 and X^2 are each O;
$R.a^3$ is H;
each of $R.a^1$ and $R.a^2$ is n-propyl;

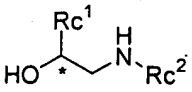
$R.a^4$ is -p- substituted phenyl wherein the substituent is heteroalkyl amide amine; and includes L which is a single bond or is $C_{1\text{-}50}$ alkyl optionally substituted by C_1 alkyl and including the formula $-(CH_2)_n$ where n is 3 to 8, optionally including one or more heteroatoms –O;

Lig.b comprises linking functionality J_L which is amine, and is



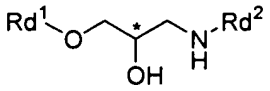
wherein ring substituents $X.b^1$ and $X.b^2$ are each OH;
ring heteroatom $X.b^3$ is -O- ;
Rb^1 is CONHEt or CH_2OH;
and each of $R.b^2$ and $R.b^3$ is H;
Rb^4 is H;
Rb^5 comprises linking functionality J_T which is amino, and linker L.b selected from saturated $C_{1\text{-}12}$ aliphatic and $C_{6\text{-}24}$ aromatic, optionally substituted by one or more C_1 alkyl and optionally including one or more heteroatoms O or cyclic groups;

Lig.c comprises linking functionality J_L which is amine and is

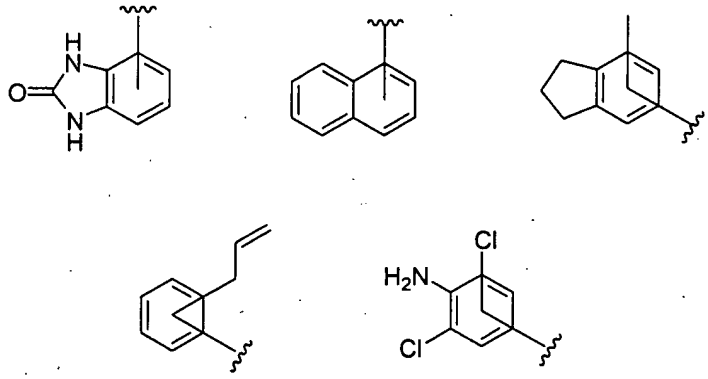


as a racemate or as one of its optically active isomers wherein * indicates an optically active centre,
Rc^1 is m-, p- dihydroxyphenyl; and
Rc^2 comprises linking functionality J_T which is amine, and linker L.c which is selected from C_{1-12} straight chain alkyl, C_{6-12} cycloalkyl or aryl and combinations thereof optionally comprising one or more heteroatoms O and optionally substituted by C_1 aliphatic;

or Lig.d comprises a linking functionality J_L which is amine and is



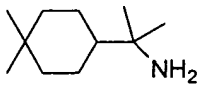
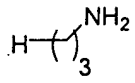
as a racemate or as one of its optically active isomers wherein * indicates an optically active centre,
Rd^1 is selected from the structures



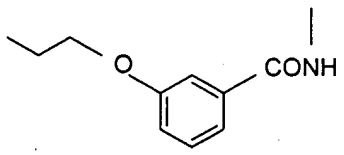
and a substituted C_{1-20} spiro aromatic ring system comprising a single aromatic ring and a heteroaryl and optionally halo substituted; and

Rd^2 comprises linking functionality J_T which is amine, and linker L.d which is selected from C_{1-12} straight chain alkyl, C_{6-12} cycloalkyl or aryl and combinations thereof optionally comprising one or more heteroatoms O and optionally substituted by C_1 aliphatic; or Rd^2 is C_{1-6} straight chain alkyl including ether O and substituted by C_{6-10} aryl which is OH and oxo substituted and comprises linker L.d as hereinbefore defined.

38. (original) Library as claimed in claim 37 wherein
$R.a^4$, $R.b^5$ or $R.c^2$ or $R.d^2$ comprises linking functionality J_T which is amino, and linker L.a, L.b, L.c or L.d selected from $(CH_2)m$ wherein m is 3, 4, 6 or 8 or is in the range 3 to 8 or 2 to 12 optionally including one or more substituents C_1, or J_L L J_T is mono or polyethylene glycol diamine, or L.a is a single bond; or
$R.c^2$ or $R.d^2$ comprises linking functionality J_T which is amino, and linker L.c or L.d selected from $C(CH_3)_2CH_2Ph$ and mono amino menthane or the structure

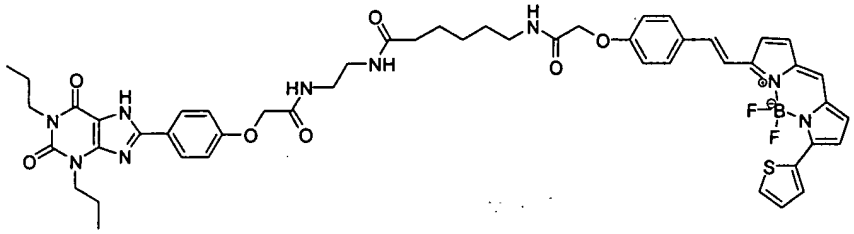
or Rd^2 comprises the following OH substituted aryl structure wherein linking functionality J_L is shown as amine, Ld is as hereinabove defined and includes J_T which is amine:



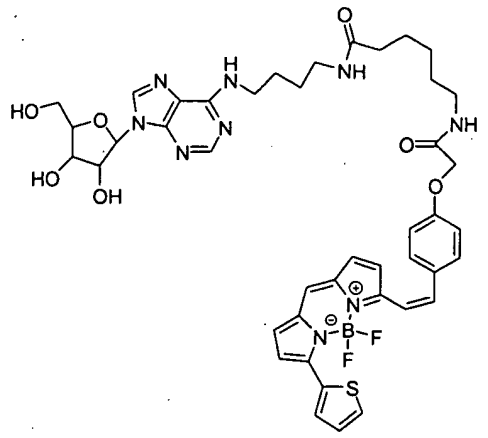
39. (currently amended) Library as claimed in Claim 37 ~~or 38~~ wherein Fl is selected from any red, near ir or blue dye.

40. (currently amended) Library as claimed in Claim 37 ~~or 38~~ wherein Fl is selected from BODIPY 630/650 X and BODIPY 630/650.

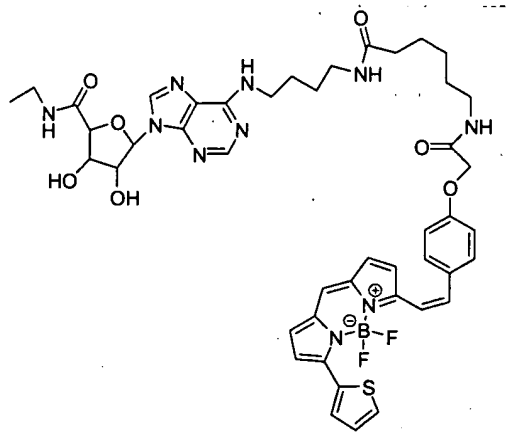
41. (currently amended) Library as claimed in ~~any of the preceding Claims~~ claim 40 comprising a compound selected from the following structures wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers:



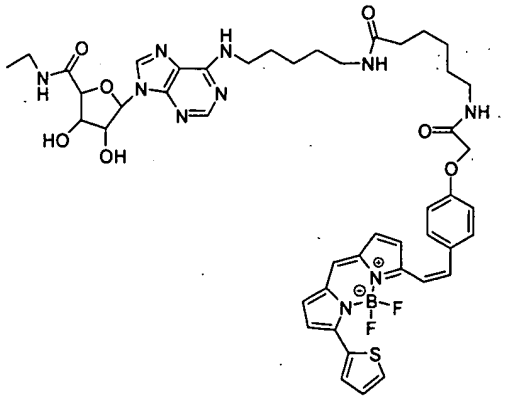
XAC – BODIPY 630/650 X



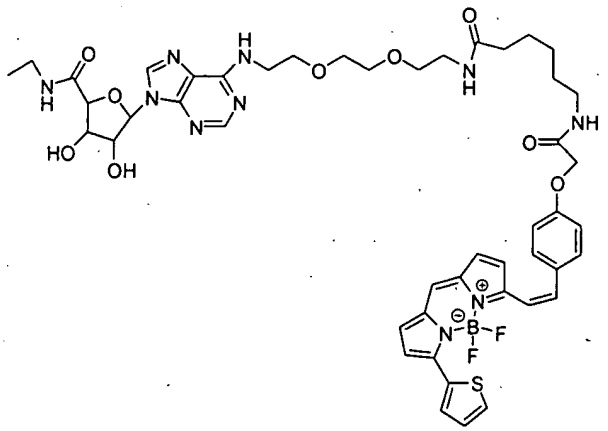
ABA-BY630



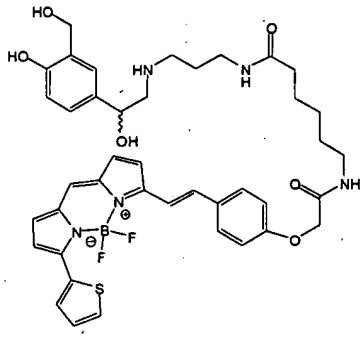
ABEA-BY630



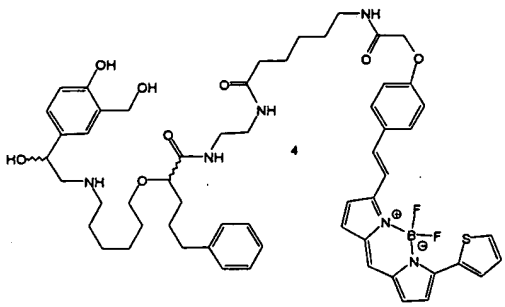
APEA-BY 630



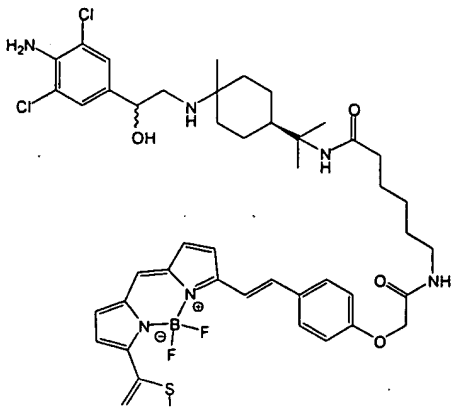
ABIPEA – BY630



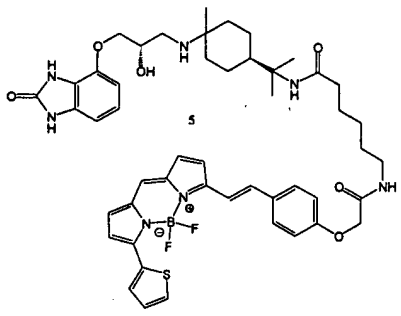
and



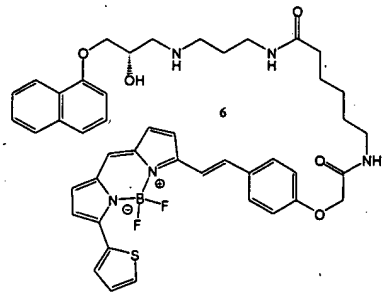
Salmeterol BY 630/650



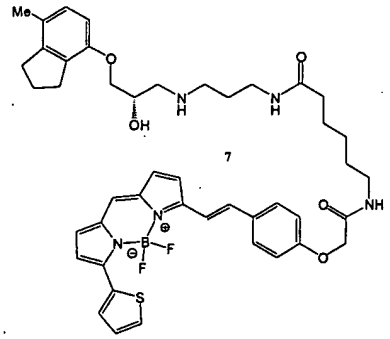
Clenbuterol BY 630/650



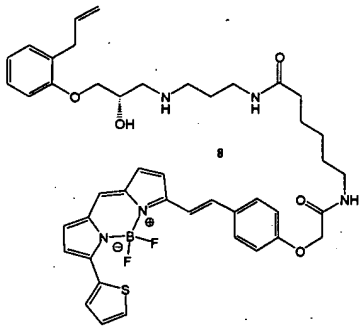
CGP12177-BY 630/650



Propranolol BY630/650



ICI118551-BY630/650



Alprenolol-BY630/650

42. (currently amended) Compound as claimed in Claim 21 of the formula

Lig J_L L J_T Fl

wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers

wherein Fl is selected from dyes in particular including fluorescein, fluorescein derivatives including FITC, and fluorescein-like molecules including Oregon Green™ and its derivatives, Texas red™, 7-nitrobenz-2-oxa-1,3-diazole (NBD) and derivatives thereof, coumarin and derivatives, naphthalene including derivatives of dansyl chloride or its analogues or derivatives, Cascade Blue™, EvoBlue and fluorescent derivatives thereof, pyrenes and pyridyloxazole derivatives, the cyanine dyes, the dyomics (DY dyes and ATTO dyes) and fluorescent derivatives thereof, the Alexafluor dyes and derivatives, BDI dyes including the commercially available Bodipy™ dyes, erythosin, eosin, pyrenes, anthracenes, acridines, fluorescent phycobiliproteins and their conjugates and fluoresceinated microbeads, Rhodamine and fluorescent derivatives thereof including Rhodamine Green™ including the tetramethylrhodamines, X-rhodamines and Texas Red derivatives, and Rhodol

Green™, coupled to amine groups using the isocyanate, succinimidyl ester or dichlorotriazinyl-reactive groups;
and
wherein Lig J_L L J_T is selected from the formulae Lig.a, Lig.b, Lig.c and Lig.d wherein:

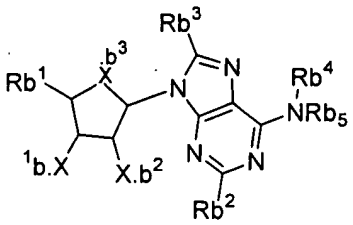
Lig.a comprises linking functionality J_L which is amine, and is of the formula, in either of the following forms given:

Lig.a $^{1}_{m}$

wherein Ra^4 comprises linking functionality J_L and J_T which is amine;
X^1 and X^2 are each O;
$R.a^3$ is H;
each of $R.a^1$ and $R.a^2$ is n-propyl;

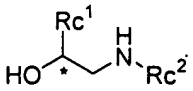
$R.a^4$ is p- substituted phenyl wherein the substituent is heteroalkyl amide amine; and includes L which is a single bond or is $C_{1\text{-}50}$ alkyl optionally substituted by C_1 alkyl and including the formula $-(CH_2)_n$ where n is 3 to 8, optionally including one or more heteroatoms –O;

Lig.b comprises linking functionality J_L which is amine, and is



wherein ring substituents $X.b^1$ and $X.b^2$ are each OH;
ring heteroatom $X.b^3$ is -O- ;
Rb^1 is CONHEt or CH_2OH;
and each of $R.b^2$ and $R.b^3$ is H;
Rb^4 is H;
Rb^5 comprises linking functionality J_T which is amino, and linker L.b selected from saturated $C_{1\text{-}12}$ aliphatic and $C_{6\text{-}24}$ aromatic, optionally substituted by one or more C_1 alkyl and optionally including one or more heteroatoms O or cyclic groups;

Lig.c comprises linking functionality J_L which is amine and is

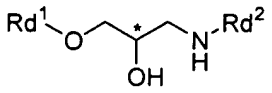


as a racemate or as one of its optically active isomers wherein * indicates an optically active centre,

Rc^1 is m-, p- dihydroxyphenyl; and

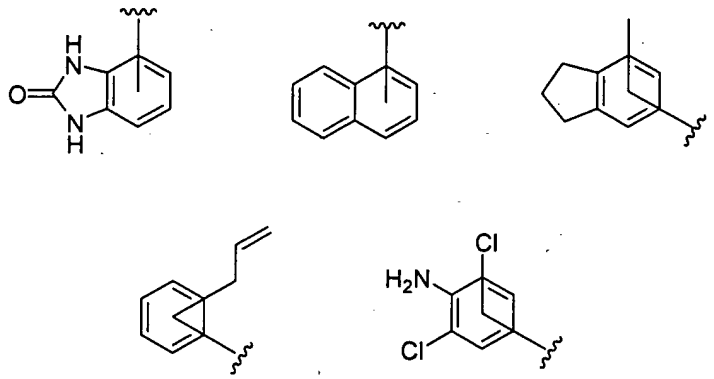
Rc^2 comprises linking functionality J_T which is amine, and linker L.c which is selected from C_{1-12} straight chain alkyl, C_{6-12} cycloalkyl or aryl and combinations thereof optionally comprising one or more heteroatoms O and optionally substituted by C_1 aliphatic;

or Lig.d comprises a linking functionality J_L which is amine and is



as a racemate or as one of its optically active isomers wherein * indicates an optically active centre,

Rd^1 is selected from the structures



and a substituted C_{1-20} spiro aromatic ring system comprising a single aromatic ring and a heteroaryl and optionally halo substituted; and

Rd^2 comprises linking functionality J_T which is amine, and linker L.d which is selected from C_{1-12} straight chain alkyl, C_{6-12} cycloalkyl or aryl and combinations thereof optionally comprising one or more heteroatoms O and optionally substituted by C_1 aliphatic; or Rd^2 is C_{1-6} straight chain alkyl including ether O and substituted by C_{6-10} aryl which is OH and oxo substituted and comprises linker L.d as hereinbefore defined,

with the proviso that the compound $JL_m\ L\ T_{Tm}$ is ~~as hereinbefore defined in Claim 8~~ is of formula

$J\ Aq_L\ R_L\ J''$

wherein each of J and J'' is amine or –O-, A is CH_2CH_2O, q_L is 1-30 or 31 to 300 and R_L is CH_2CH_2

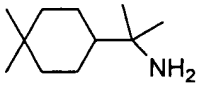
or of formula

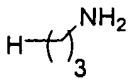
$J\ Aq_L\ R_L(A'J')\ J''$

wherein each of J, J' and J'' independently is amine, –O or a single bond, q_L is 1, 2 or 3 -30 or 31 to 300 and A is CH_2CH_2O or $HNCH_2CO$ or q_L is 1 and A is C(O) or $(CH_2)_{1-8}$ or q_L is 0, R_L is CH or CH_2CH, $q_{L'}$ is 0 or $q_{L'}$ is 1 and A' is CH_2 and $q_{L''}$ is 0 preferably

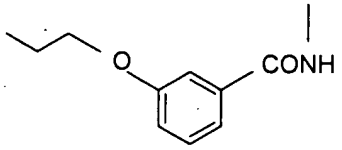
$O(CH_2CH_2O)q_LCH_2CH_2NH$, $O(CH_2CH_2O)q_LCH_2CH(CH_2NH)NH$, $OCH(CH_2NH)NH$, $-CH(CH_2NH)NH$, -C(O) NH-, $-(CH_2)_{1-8}-$ or $(-HNCH_2CO-)_{1-3}$ (= $-gly_{1-3}-$) - and wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers ~~a compound excluded in Claim 18~~.

43. (currently amended) Compound as claimed in Claim 42 wherein $R.a^4$, $R.b^5$ or $R.c^2$ or $R.d^2$ comprises linking functionality J_T which is amino, and linker L.a, L.b, L.c or L.d selected from $(CH_2)m$ wherein m is 3, 4, 6 or 8 or is in the range 3 to 8 or 2 to 12 optionally including one or more substituents C_1, or J_L L J_T is mono or polyethylene glycol diamine, or L.a is a single bond; or
$R.c^2$ or $R.d^2$ comprises linking functionality J_T which is amino, and linker L.c or L.d selected from $C(CH_3)_2CH_2Ph$ and mono amino menthane or the structure





or Rd^2 comprises the following OH substituted aryl structure wherein linking functionality J_L is shown as amine, Ld is as hereinabove defined and includes J_T which is amine:

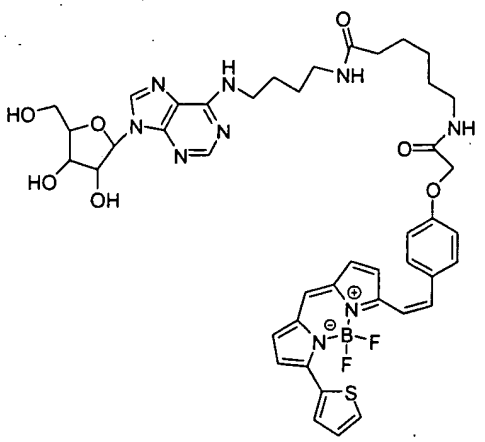


with the proviso that when Lig is XAC ie in Lig.a when each of $R.a^1$ and $R.a^2$ is propyl, $R.a^3$ is H and $R.a^4$ is $-Ph-OCH_2CONH(CH_2)_2NH-$, and L is a single bond Fl is not BODIPY ™ 630/650 X; or
b) when Lig is ABEA, ie m is 4 and L is a single bond Fl is not BODIPY™ 630/650 X. ~~the compound is not a compound excluded in Claim 21~~.

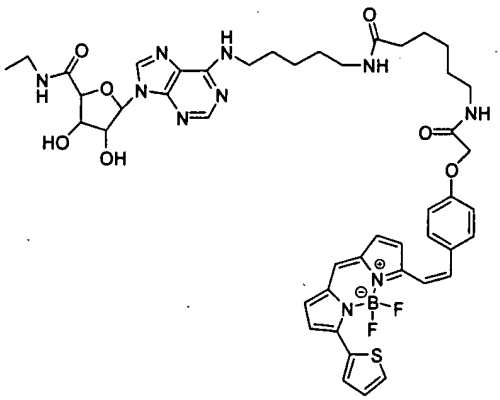
44. (currently amended) Compound as claimed in Claim 42 ~~or 43~~ wherein Fl is selected from any red, near ir or blue dye.

45. (currently amended) Compound as claimed in Claim 42 ~~or 43~~ wherein Fl is selected from BODIPY 630/650 X and BODIPY 630/650.

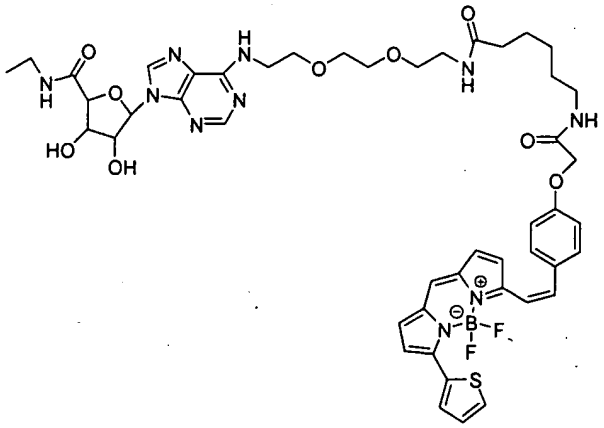
46. (original) Compound selected from the structures wherein any optically active fluorescent ligand is present as a racemate or as one of its optically active isomers:



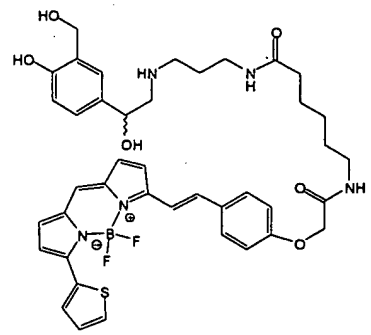
ABA-BY630



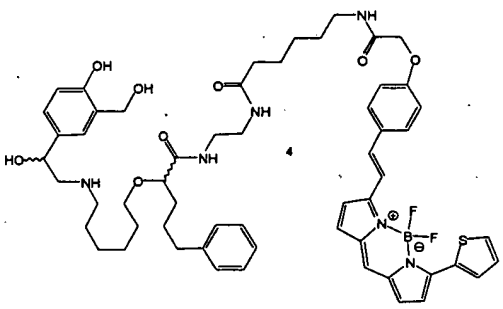
APEA-BY 630



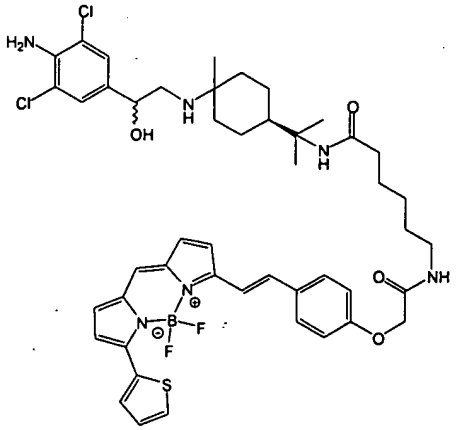
ABIPEA – BY630



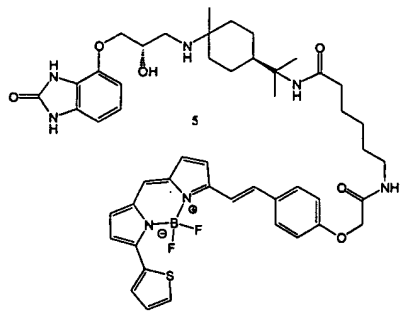
and



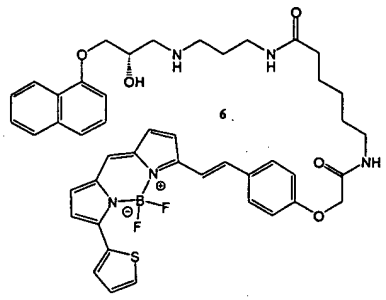
Salmeterol BY 630/650



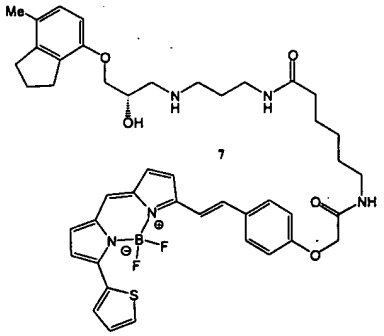
Clenbuterol BY 630/650



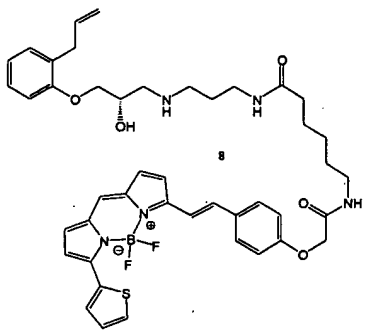
CGP12177-BY 630/650



Propranolol BY630/650

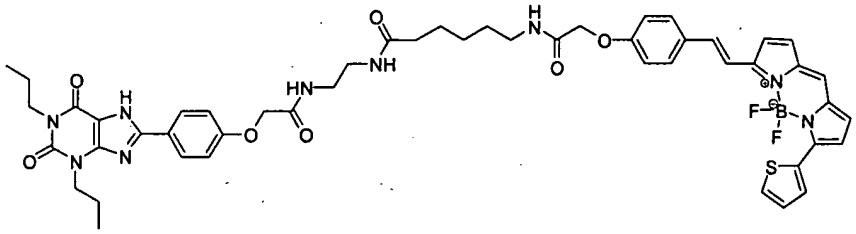


ICI118551-BY630/650



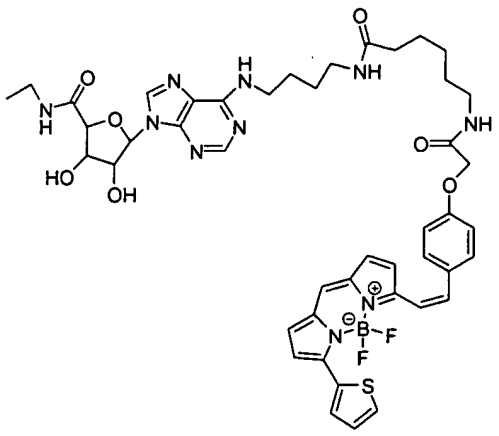
Alprenolol-BY630/650

and optionally additionally



XAC – BODIPY 630/650 X

or



ABEA-BY630.